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DOCUMENT TYPE: CODEN: BIOJAU. ISSN: 0006-3495.
Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 3 Jul 2002
Last Updated on STN: 3 Jul 2002

=> d his

(FILE 'HOME' ENTERED AT 12:49:11 ON 10 FEB 2007)

FILE 'MEDLINE, BIOSIS' ENTERED AT 12:49:32 ON 10 FEB 2007
L1 0 S (INTRACELLULAR RECOGNITION MOLECULE) AND (PEPTIDE APTAMER)
L2 2 S (TRX AND TRX-LIKE PROTEIN)

=> s (thioredoxin and TRX-like protein)
L3 1 (THIOREDOXIN AND TRX-LIKE PROTEIN)

=> d l3 ti abs ibib tot

L3 ANSWER 1 OF 1 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Dim2, a new TRX-like protein implicated in
cell cycle progression.

ACCESSION NUMBER: 2005:301677 BIOSIS
DOCUMENT NUMBER: PREV200510095702
TITLE: Dim2, a new TRX-like protein
implicated in cell cycle progression.
AUTHOR(S): Simeoni, F. [Reprint Author]; Bello, P.; Gondeau, C.;
Neyroz, P.; Tainer, J.; Heitz, F.; Divita, G.
CORPORATE SOURCE: CNRS, CRBM, F-34033 Montpellier, France
SOURCE: Molecular Biology of the Cell, (NOV 2004) Vol. 15, No.
Suppl. S, pp. 369A.
Meeting Info.: 44th Annual Meeting of the
American-Society-for-Cell-Biology. Washington, DC, USA.
December 04 -08, 2004. Amer Soc Cell Biol.
CODEN: MBCEEV. ISSN: 1059-1524.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 15 Aug 2005
Last Updated on STN: 15 Aug 2005

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(FILE 'HOME' ENTERED AT 12:49:11 ON 10 FEB 2007)

FILE 'MEDLINE, BIOSIS' ENTERED AT 12:49:32 ON 10 FEB 2007
L1 0 S (INTRACELLULAR RECOGNITION MOLECULE) AND (PEPTIDE APTAMER)
L2 2 S (TRX AND TRX-LIKE PROTEIN)
L3 1 S (THIOREDOXIN AND TRX-LIKE PROTEIN)

=> s thioredoxin
L4 9702 THIOREDOXIN

=> d 14 and 11
L1 IS NOT VALID HERE
For an explanation, enter "HELP DISPLAY".

=> d his

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FILE 'MEDLINE, BIOSIS' ENTERED AT 12:49:32 ON 10 FEB 2007

L1 0 S (INTRACELLULAR RECOGNITION MOLECULE) AND (PEPTIDE APTAMER)
L2 2 S (TRX AND TRX-LIKE PROTEIN)
L3 1 S (THIOREDOXIN AND TRX-LIKE PROTEIN)
L4 9702 S THIOREDOXIN

=> s 14 and (cdk2)
L5 7 L4 AND (CDK2)

=> d 15 ti abs ibib tot

L5 ANSWER 1 OF 7 MEDLINE on STN

TI Production of soluble mammalian proteins in Escherichia coli: identification of protein features that correlate with successful expression.

AB BACKGROUND: In the search for generic expression strategies for mammalian protein families several bacterial expression vectors were examined for their ability to promote high yields of soluble protein. Proteins studied included cell surface receptors (Ephrins and Eph receptors, CD44), kinases (EGFR-cytoplasmic domain, CDK2 and 4), proteases (MMP1, CASP2), signal transduction proteins (GRB2, RAF1, HRAS) and transcription factors (GATA2, Fli1, Trp53, Mdm2, JUN, FOS, MAD, MAX). Over 400 experiments were performed where expression of 30 full-length proteins and protein domains were evaluated with 6 different N-terminal and 8 C-terminal fusion partners. Expression of an additional set of 95 mammalian proteins was also performed to test the conclusions of this study. RESULTS: Several protein features correlated with soluble protein expression yield including molecular weight and the number of contiguous hydrophobic residues and low complexity regions. There was no relationship between successful expression and protein pI, grand average of hydropathicity (GRAVY), or sub-cellular location. Only small globular cytoplasmic proteins with an average molecular weight of 23 kDa did not require a solubility enhancing tag for high level soluble expression.

Thioredoxin (Trx) and maltose binding protein (MBP) were the best N-terminal protein fusions to promote soluble expression, but MBP was most effective as a C-terminal fusion. 63 of 95 mammalian proteins expressed at soluble levels of greater than 1 mg/l as N-terminal H10-MBP fusions and those that failed possessed, on average, a higher molecular weight and greater number of contiguous hydrophobic amino acids and low complexity regions. CONCLUSIONS: By analysis of the protein features identified here, this study will help predict which mammalian proteins and domains can be successfully expressed in E. coli as soluble product and also which are best targeted for a eukaryotic expression system. In some cases proteins may be truncated to minimise molecular weight and the numbers of contiguous hydrophobic amino acids and low complexity regions to aid soluble expression in E. coli.

ACCESSION NUMBER: 2005032544 MEDLINE

DOCUMENT NUMBER: PubMed ID: 15598350

TITLE: Production of soluble mammalian proteins in Escherichia coli: identification of protein features that correlate with successful expression.

AUTHOR: Dyson Michael R; Shadbolt S Paul; Vincent Karen J; Perera Rajika L; McCafferty John

CORPORATE SOURCE: The Atlas of Gene Expression Project, The Wellcome Trust Sanger Institute, Wellcome Trust Genome Campus, Hinxton, Cambridge, CB10 1SA, UK.. mrd@sanger.ac.uk

SOURCE: BMC biotechnology [electronic resource], (2004 Dec 14) Vol. 4, pp. 32. Electronic Publication: 2004-12-14. Journal code: 101088663. E-ISSN: 1472-6750.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200601
ENTRY DATE: Entered STN: 25 Jan 2005
Last Updated on STN: 14 Dec 2005
Entered Medline: 26 Jan 2006

L5 ANSWER 2 OF 7 MEDLINE on STN
TI Engineered protein scaffolds for molecular recognition.
AB The use of so-called protein scaffolds has recently attracted considerable attention in biochemistry in the context of generating novel types of ligand receptors for various applications in research and medicine. This development started with the notion that immunoglobulins owe their function to the composition of a conserved framework region and a spatially well-defined antigen-binding site made of peptide segments that are hypervariable both in sequence and in conformation. After the application of antibody engineering methods along with library techniques had resulted in first successes in the selection of functional antibody fragments, several laboratories began to exploit other types of protein architectures for the construction of practically useful binding proteins. Properties like small size of the receptor protein, stability and ease of production were the focus of this work. Hence, among others, single domains of antibodies or of the immunoglobulin superfamily, protease inhibitors, helix-bundle proteins, disulphide-knotted peptides and lipocalins were investigated. Recently, the scaffold concept has even been adopted for the construction of enzymes. However, it appears that not all kinds of polypeptide fold which may appear attractive for the engineering of loop regions at a first glance will indeed permit the construction of independent ligand-binding sites with high affinities and specificities. This review will therefore concentrate on the critical description of the structural properties of experimentally tested protein scaffolds and of the novel functions that have been achieved on their basis, rather than on the methodology of how to best select a particular mutant with a certain activity. An overview will be provided about the current approaches, and some emerging trends will be identified. (c) 2000 John Wiley & Sons, Ltd. Abbreviations used: ABD albumin-binding domain of protein G APPI Alzheimer's amyloid beta-protein precursor inhibitor BBP bilin-binding protein BPTI bovine (or basic) pancreatic trypsin inhibitor BSA bovine serum albumin CBD cellulose-binding domain of cellobiohydrolase I CD circular dichroism Cdk2 human cyclin-dependent kinase 2 CDR complementarity-determining region CTLA-4 human cytotoxic T-lymphocyte associated protein-4 FN3 fibronectin type III domain GSH glutathione GST glutathione S-transferase hIL-6 human interleukin-6 HSA human serum albumin IC(50) half-maximal inhibitory concentration Ig immunoglobulin IMAC immobilized metal affinity chromatography K(D) equilibrium constant of dissociation K(i) equilibrium dissociation constant of enzyme inhibitor LACI-D1 human lipoprotein-associated coagulation inhibitor pIII gene III minor coat protein from filamentous bacteriophage f1 PCR polymerase-chain reaction PDB Protein Data Bank PSTI human pancreatic secretory trypsin inhibitor RBP retinol-binding protein SPR surface plasmon resonance TrxA E. coli thioredoxin

ACCESSION NUMBER: 2000424395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10931555
TITLE: Engineered protein scaffolds for molecular recognition.
AUTHOR: Skerra A
CORPORATE SOURCE: Lehrstuhl fur Biologische Chemie, Technische Universitat Munchen, D-85350 Freising-Weihenstephan, Germany.
Skerra@Weihenstephan.de
SOURCE: Journal of molecular recognition : JMR, (2000 Jul-Aug) Vol. 13, No. 4, pp. 167-87. Ref: 115
Journal code: 9004580. ISSN: 0952-3499.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 22 Sep 2000
Last Updated on STN: 23 Jul 2001
Entered Medline: 14 Sep 2000

L5 ANSWER 3 OF 7 MEDLINE on STN
TI Selenium metabolism, selenoproteins and mechanisms of cancer prevention: complexities with thioredoxin reductase.
AB Numerous studies in animal models and more recent studies in humans have demonstrated cancer chemopreventive effects with Se. There is extensive evidence that monomethylated forms of Se are critical metabolites for chemopreventive effects of Se. Induction of apoptosis in transformed cells is an important chemopreventive mechanism. Apoptosis can be triggered by micromolar levels of monomethylated forms of Se independent of DNA damage and in cells having a null p53 phenotype. Cell cycle protein kinase cdk2 and protein kinase C are strongly inhibited by various forms of Se. Inhibitory mechanisms involving modification of cysteine residues in proteins by Se have been proposed that involve formation of Se adducts of the selenotrisulfide (S-Se-S) or selenenylsulfide (S-Se) type or catalysis of disulfide formation. Selenium may facilitate reactions of protein cysteine residues by the transient formation of more reactive S-Se intermediates. A novel chemopreventive mechanism is proposed involving Se catalysis of reversible cysteine/disulfide transformations that occur in a number of redox-regulated proteins, including transcription factors. A time-limited activation mechanism for such proteins, with deactivation facilitated by Se, would allow normalization of critical cellular processes in the early stages of transformation. There is uncertainty at the present time regarding the role of selenoproteins in chemoprevention model systems where supranutritional levels of Se are employed. Mammalian thioredoxin reductase is one selenoprotein that shows increased activity with Se supplementation in the nutritional to supranutritional range. Enhanced thioredoxin reduction could have beneficial effects in oxidative stress, but possible adverse effects are considered. Other functions of thioredoxin reductase may be relevant to cell signaling pathways. The functional status of the thioredoxin/thioredoxin reductase system during in vivo chemoprevention with Se has not been established. Some in vitro studies have shown inhibitory effects of Se on the thioredoxin system correlated with growth inhibition by Se. A potential inactivating mechanism for thioredoxin reductase or other selenoenzymes involving formation of a stable diselenide form resistant to reduction is discussed. New aspects of Se biochemistry and possible functions of new selenoproteins in chemoprevention are described.

ACCESSION NUMBER: 1999400568 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10469608
TITLE: Selenium metabolism, selenoproteins and mechanisms of cancer prevention: complexities with thioredoxin reductase.
AUTHOR: Ganther H E
CORPORATE SOURCE: Department of Nutritional Sciences, University of Wisconsin, 1415 Linden Drive, Madison, WI 53706, USA..
hganther@facstaff.wisc.edu
CONTRACT NUMBER: CA 45164 (NCI)
SOURCE: Carcinogenesis, (1999 Sep) Vol. 20, No. 9, pp. 1657-66.
Ref: 86
Journal code: 8008055. ISSN: 0143-3334.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199909
ENTRY DATE: Entered STN: 12 Oct 1999

Last Updated on STN: 3 Mar 2000
Entered Medline: 30 Sep 1999

L5 ANSWER 4 OF 7 MEDLINE on STN
TI Genetic selection of peptide aptamers that recognize and inhibit cyclin-dependent kinase 2.
AB A network of interacting proteins controls the activity of cyclin-dependent kinase 2 (Cdk2) (refs 1,2) and governs the entry of higher eukaryotic cells into S phase. Analysis of this and other genetic regulatory networks would be facilitated by intracellular reagents that recognize specific targets and inhibit specific network connections. We report here the expression of a combinatorial library of constrained 20-residue peptides displayed by the active-site loop of *Escherichia coli* thioredoxin, and the use of a two-hybrid system to select those that bind human Cdk2. These peptide aptamers were designed to mimic the recognition function of the complementarity-determining regions of immunoglobulins. The aptamers recognized different epitopes on the Cdk2 surface with equilibrium dissociation constant in the nanomolar range; those tested inhibited Cdk2 activity. Our results show that peptide aptamers bear some analogies with monoclonal antibodies, with the advantages that they are isolated together with their coding genes, that their small size should allow their structures to be solved, and that they are designated to function inside cells.

ACCESSION NUMBER: 96195065 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8606778
TITLE: Genetic selection of peptide aptamers that recognize and inhibit cyclin-dependent kinase 2.
AUTHOR: Colas P; Cohen B; Jessen T; Grishina I; McCoy J; Brent R
CORPORATE SOURCE: Department of Molecular Biology, Massachusetts General Hospital, Boston, Massachusetts 02114, USA.
SOURCE: *Nature*, (1996 Apr 11) Vol. 380, No. 6574, pp. 548-50.
Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199605
ENTRY DATE: Entered STN: 31 May 1996
Last Updated on STN: 6 Feb 1998
Entered Medline: 20 May 1996

L5 ANSWER 5 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Production of soluble mammalian proteins in *Escherichia coli*: identification of protein features that correlate with successful expression.
AB Background: In the search for generic expression strategies for mammalian protein families several bacterial expression vectors were examined for their ability to promote high yields of soluble protein. Proteins studied included cell surface receptors (Ephrins and Eph receptors, CD44), kinases (EGFR-cytoplasmic domain, CDK2 and 4), proteases (MMP1, CASP2), signal transduction proteins (GRB2, RAF1, HRAS) and transcription factors (GATA2, Fli1, Trp53, Mdm2, JUN, FOS, MAD, MAX). Over 400 experiments were performed where expression of 30 full-length proteins and protein domains were evaluated with 6 different N-terminal and 8 C-terminal fusion partners. Expression of an additional set of 95 mammalian proteins was also performed to test the conclusions of this study. Results: Several protein features correlated with soluble protein expression yield including molecular weight and the number of contiguous hydrophobic residues and low complexity regions. There was no relationship between successful expression and protein pI, grand average of hydropathicity (GRAVY), or sub-cellular location. Only small globular cytoplasmic proteins with an average molecular weight of 23 kDa did not require a solubility enhancing tag for high level soluble expression. Thioredoxin (Trx) and maltose binding protein (MBP) were the best

N-terminal protein fusions to promote soluble expression, but MBP was most effective as a C-terminal fusion. 63 of 95 mammalian proteins expressed at soluble levels of greater than 1 mg/l as N-terminal H10-MBP fusions and those that failed possessed, on average, a higher molecular weight and greater number of contiguous hydrophobic amino acids and low complexity regions. Conclusions: By analysis of the protein features identified here, this study will help predict which mammalian proteins and domains can be successfully expressed in *E. coli* as soluble product and also which are best targeted for a eukaryotic expression system. In some cases proteins may be truncated to minimise molecular weight and the numbers of contiguous hydrophobic amino acids and low complexity regions to aid soluble expression in *E. coli*.

ACCESSION NUMBER: 2005:159023 BIOSIS

DOCUMENT NUMBER: PREV200500160892

TITLE: Production of soluble mammalian proteins in *Escherichia coli*: identification of protein features that correlate with successful expression.

AUTHOR(S): Dyson, Michael R. [Reprint Author]; Shadbolt, S. Paul; Vincent, Karen J.; Perera, Rajika L.; McCafferty, John

CORPORATE SOURCE: Atlas Gene Express Project, Wellcome Trust Sanger Inst, Wellcome Trust Genome Campus, Cambridge, CB10 1SA, UK
mrd@sanger.ac.uk; ps3@sanger.ac.uk; kjk@sanger.ac.uk;
rlp@sanger.ac.uk; jm9@sanger.ac.uk

SOURCE: BMC Biotechnology, (December 14 2004) Vol. 4, No. December 14. print.

E-ISSN: 1472-6750 (ISSN online).

DOCUMENT TYPE: Article

LANGUAGE: English

ENTRY DATE: Entered STN: 27 Apr 2005

Last Updated on STN: 27 Apr 2005

L5 ANSWER 6 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Selenium metabolism, selenoproteins and mechanisms of cancer prevention:
Complexities with thioredoxin reductase.

AB Numerous studies in animal models and more recent studies in humans have demonstrated cancer chemopreventive effects with Se. There is extensive evidence that monomethylated forms of Se are critical metabolites for chemopreventive effects of Se. Induction of apoptosis in transformed cells is an important chemopreventive mechanism. Apoptosis can be triggered by micromolar levels of monomethylated forms of Se independent of DNA damage and in cells having a null p53 phenotype. Cell cycle protein kinase cdk2 and protein kinase C are strongly inhibited by various forms of Se. Inhibitory mechanisms involving modification of cysteine residues in proteins by Se have been proposed that involve formation of Se adducts of the selenotrisulfide (S-Se-S) or selenenylsulfide (S-Se) type or catalysis of disulfide formation. Selenium may facilitate reactions of protein cysteine residues by the transient formation of more reactive S-Se intermediates. A novel chemopreventive mechanism is proposed involving Se catalysis of reversible cysteine/disulfide transformations that occur in a number of redox-regulated proteins, including transcription factors. A time-limited activation mechanism for such proteins, with deactivation facilitated by Se, would allow normalization of critical cellular processes in the early stages of transformation. There is uncertainty at the present time regarding the role of selenoproteins in chemoprevention model systems where supranutritional levels of Se are employed. Mammalian thioredoxin reductase is one selenoprotein that shows increased activity with Se supplementation in the nutritional to supranutritional range. Enhanced thioredoxin reduction could have beneficial effects in oxidative stress, but possible adverse effects are considered. Other functions of thioredoxin reductase may be relevant to cell signaling pathways. The functional status of the thioredoxin/thioredoxin reductase system during *in vivo* chemoprevention with Se has not been established. Some *in vitro* studies have shown inhibitory

effects of Se on the thioredoxin system correlated with growth inhibition by Se. A potential inactivating mechanism for thioredoxin reductase or other selenoenzymes involving formation of a stable diselenide form resistant to reduction is discussed. New aspects of Se biochemistry and possible functions of new selenoproteins in chemoprevention are described.

ACCESSION NUMBER: 1999:480208 BIOSIS

DOCUMENT NUMBER: PREV199900480208

TITLE: Selenium metabolism, selenoproteins and mechanisms of cancer prevention: Complexities with thioredoxin reductase.

AUTHOR(S): Ganther, Howard E. [Reprint author]

CORPORATE SOURCE: Department of Nutritional Sciences, University of Wisconsin, 1415 Linden Drive, Madison, WI, 53706, USA

SOURCE: Carcinogenesis (Oxford), (Sept., 1999) Vol. 20, No. 9, pp. 1657-1666. print.

CODEN: CRNGDP. ISSN: 0143-3334.

DOCUMENT TYPE: Article
General Review; (Literature Review)

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Nov 1999

Last Updated on STN: 9 Nov 1999

L5 ANSWER 7 OF 7 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
TI Genetic selection of peptide aptamers that recognize and inhibit cyclin-dependent kinase 2.

AB A network of interacting proteins controls the activity of cyclin-independent kinase 2 (Cdk2) (refs 1, 2) and governs the entry of higher eukaryotic cells into S phase. Analysis of this and other genetic regulatory networks would be facilitated by intracellular reagents that recognize specific targets and inhibit specific network connections. We report here the expression of a combinatorial library of constrained 20-residue peptides displayed by the active-site loop of *Escherichia coli* thioredoxin, and the use of a two-hybrid system to select those that bind human Cdk2. These peptide aptamers were designed to mimic the recognition function of the complementarity-determining regions of immunoglobulins. The aptamers recognized different epitopes on the Cdk2 surface with equilibrium dissociation constant in the nanomolar range; those tested inhibited Cdk2 activity. Our results show that peptide aptamers bear some analogies with monoclonal antibodies, with the advantages that they are isolated together with their coding genes, that their small size should allow their structures to be solved, and that they are designated to function inside cells.

ACCESSION NUMBER: 1996:218529 BIOSIS

DOCUMENT NUMBER: PREV199698774658

TITLE: Genetic selection of peptide aptamers that recognize and inhibit cyclin-dependent kinase 2.

AUTHOR(S): Colas, Pierre; Cohen, Barak; Jessen, Timm; Grishina, Irina; McCoy, John; Brent, Roger [Reprint author]

CORPORATE SOURCE: Dep. Mol. Biol., Massachusetts General Hosp., 50 Blossom St., Boston, MA 02114, USA

SOURCE: Nature (London), (1996) Vol. 380, No. 6574, pp. 548-550.
CODEN: NATUAS. ISSN: 0028-0836.

DOCUMENT TYPE: Article
LANGUAGE: English

ENTRY DATE: Entered STN: 8 May 1996

Last Updated on STN: 10 Jun 1996

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<u>L1</u>	(thioredoxin and TRX-like protein)	177593	<u>L1</u>

END OF SEARCH HISTORY